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<120> Regulation of Human Transient Receptor Potential Channel

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<150> PCT/EP03/03713

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<150> US 60/372,899

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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
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Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
Page 22

180

185

190

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755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
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Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
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Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn Gly Gln Leu Lys Leu  
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Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
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Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
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Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys  
1010 1015 1020

Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn  
1025 1030 1035

Glu Asp Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn  
1040 1045 1050

Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu  
1055 1060 1065

Met Arg His Arg Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu  
1070 1075 1080

Lys Gly Leu Leu Lys Glu Ile Ala Asn Lys Ile Lys  
1085 1090 1095

<210> 16  
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<222> (867)..(867)  
<223> Xaa can be any naturally occurring amino acid

<400> 16

Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
35. 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu  
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp.  
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser

385

390

395

400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
625 630 635 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
645 650 655

Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val  
755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr  
770 775 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe  
785 790 795 800

Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu  
805 810 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu  
820 825 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile  
835 840 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Leu Phe Leu  
850 855 860

Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu  
865 870 875 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr  
885 890 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly  
900 905 910

Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys  
915 920 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu  
930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile  
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr  
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu  
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val  
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys  
1010 1015 1020

Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn  
1025 1030 1035

Glu Asp Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn  
1040 1045 1050

Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu  
1055 1060 1065

Met Arg His Arg Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu  
1070 1075 1080

Lys Gly Leu Leu Lys Glu Ile Ala Asn Lys Ile Lys  
1085 1090 1095

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<211> 652

<212> PRT

<213> Homo sapiens

<400> 17

Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
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20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
Page 39

85

90

95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu  
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
625 630 635 640

Ala Trp Gly Gly Leu Glu His His His His His His  
645 650

<210> 18  
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<220>  
<221> misc\_feature  
<222> (867)..(867)  
<223> Xaa can be any naturally occurring amino acid

<400> 18

Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu  
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu  
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe  
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
625 630 635 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp  
645 650 655

Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln  
660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu  
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg  
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala  
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr  
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His  
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val

755

760

765

Leu Phe Cys Asp Glu Val Arg 770 775 Gln Trp Tyr Val Asn Gly Val Asn Tyr 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu 785 790 Gly Leu Phe Tyr Phe 800

Ile Ala Gly Ile Val Phe Arg Leu His Ser 805 810 Ser Asn Lys Ser Ser Leu 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu 820 825 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile 835 840 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Leu Phe Leu 850 855 860

Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu 865 870 875 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr 885 890 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly 900 905 910

Thr Thr Tyr Asp Phe Ala His Cys 915 920 Thr Phe Thr Gly Asn Glu Ser Lys 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu 930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile 945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr 965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu 980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val 995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys 1010 1015 1020

Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn 1025 1030 1035

Glu Asp Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn  
1040 1045 1050

Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu  
1055 1060 1065

Met Arg His Arg Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu  
1070 1075 1080

Lys Gly Leu Leu Lys Glu Ile Ala Asn Lys Ile Lys  
1085 1090 1095

<210> 19

<211> 652

<212> PRT

<213> Homo sapiens

<400> 19

Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr  
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Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu  
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe  
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala  
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp  
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp  
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser  
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp  
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys  
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile  
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His  
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile  
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp  
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu  
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro  
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn  
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu  
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly  
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu  
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val  
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val  
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp  
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val  
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser  
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn  
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Glu Trp Asn Gln Leu Asp Leu  
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp  
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe

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455

460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr  
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val  
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu  
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys  
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val  
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile  
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg  
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu  
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu  
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr  
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu  
625 630 635 640

Ala Trp Gly Gly Leu Glu His His His His His His  
645 650

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<211> 1104

<212> PRT

<213> Homo sapiens

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Asp Leu Ser Tyr Ser Glu Ser Asp Leu Val Asn Phe Ile Gln Ala Asn  
35 40 45

Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys Asp Ser Lys Ala Thr  
50 55 60

Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser Gln His Met Glu Gly  
65 70 75 80

Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys  
85 90 95

Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly  
100 105 110

Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile  
115 120 125

Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu  
130 135 140

Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg  
145 150 155 160

Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly  
165 170 175

Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile  
180 185 190

Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn  
195 200 205

Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp  
210 215 220

Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr  
225 230 235 240

Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Cys Ile Leu Asp Asn Asn  
245 250 255

His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr  
260 265 270

Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg  
275 280 285

Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe  
290 295 300

Ala Gln Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile  
305 310 315 320

Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly Ser Gly Gln Ile Ala  
325 330 335

Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp Ala Leu Thr Ser Ser  
340 345 350

Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro Arg Thr Val Ser Arg  
355 360 365

Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile  
370 375 380

Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys Met Glu Glu Ala Gly  
385 390 395 400

Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala Leu Tyr Lys Ala Phe  
405 410 415

Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn Gly Gln Leu Lys Leu  
420 425 430

Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn Asp Glu Ile Phe Thr  
435 440 445

Asn Asp Arg Arg Trp Glu Ser Ala Asp Leu Gln Glu Val Met Phe Thr  
450 455 460

Ala Leu Ile Lys Asp Arg Pro Lys Phe Val Arg Leu Phe Leu Glu Asn  
465 470 475 480

Gly Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu  
485 490 495

Phe Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala  
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Lys Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val  
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Ala Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp  
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Glu Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro  
545 550 555 560

Leu Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu  
565 570 575

Ser Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu  
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Gly Ala Ser Lys Leu Leu Lys Thr Leu Ala Lys Val Lys Asn Asp Ile

595

600

605

Asn Ala Ala Gly Glu Ser Glu Glu Leu Ala Asn Glu Tyr Glu Thr Arg  
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Ala Val Glu Leu Phe Thr Glu Cys Tyr Ser Ser Asp Glu Asp Leu Ala  
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Glu Gln Leu Leu Val Tyr Ser Cys Glu Ala Trp Gly Gly Ser Asn Cys  
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Leu Glu Leu Ala Val Glu Ala Thr Asp Gln His Phe Ile Ala Gln Pro  
660 665 670

Gly Val Gln Asn Phe Leu Ser Lys Gln Trp Tyr Gly Glu Ile Ser Arg  
675 680 685

Asp Thr Lys Asn Trp Lys Ile Ile Leu Cys Leu Phe Ile Ile Pro Leu  
690 695 700

Val Gly Cys Gly Phe Val Ser Phe Arg Lys Lys Pro Val Asp Lys His  
705 710 715 720

Lys Lys Leu Leu Trp Tyr Tyr Val Ala Phe Phe Thr Ser Pro Phe Val  
725 730 735

Val Phe Ser Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe  
740 745 750

Ala Tyr Val Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu  
755 760 765

Leu Val Leu Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Val Arg  
770 775 780

Gln Trp Tyr Val Asn Gly Val Asn Tyr Phe Thr Asp Leu Trp Asn Val  
785 790 795 800

Met Asp Thr Leu Gly Leu Phe Tyr Phe Ile Ala Gly Ile Val Phe Arg  
805 810 815

Leu His Ser Ser Asn Lys Ser Ser Leu Tyr Ser Gly Arg Val Ile Phe  
820 825 830

Cys Leu Asp Tyr Ile Ile Phe Thr Leu Arg Leu Ile His Ile Phe Thr  
835 840 845

Val Ser Arg Asn Leu Gly Pro Lys Ile Ile Met Leu Gln Arg Met Leu  
850 855 860

Ile Asp Val Phe Phe Phe Leu Phe Leu Phe Ala Val Trp Met Val Ala  
865 870 875 880

Phe Gly Val Ala Arg Gln Gly Ile Leu Arg Gln Asn Glu Gln Arg Trp  
885 890 895

Arg Trp Ile Phe Arg Ser Val Ile Tyr Glu Pro Tyr Leu Ala Met Phe  
900 905 910

Gly Gln Val Pro Ser Asp Val Asp Gly Thr Thr Tyr Asp Phe Ala His  
915 920 925

Cys Thr Phe Thr Gly Asn Glu Ser Lys Pro Leu Cys Val Glu Leu Asp  
930 935 940

Glu His Asn Leu Pro Arg Phe Pro Glu Trp Ile Thr Ile Pro Leu Val  
945 950 955 960

Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu Leu Val  
965 970 975

Ala Met Phe Gly Tyr Thr Val Gly Thr Val Gln Glu Asn Asn Asp Gln  
980 985 990

Val Trp Lys Phe Gln Arg Tyr Phe Leu Val Gln Glu Tyr Cys Ser Arg  
995 1000 1005

Leu Asn Ile Pro Phe Pro Phe Ile Val Phe Ala Tyr Phe Tyr Met  
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Val Val Lys Lys Cys Phe Lys Cys Cys Cys Lys Glu Lys Asn Met  
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Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp Asn Glu Thr Leu  
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Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val Lys Ile Asn  
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Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg Phe Arg  
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35 40 45

Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Ala Ser Phe Tyr Ala Ala  
50 55 60

Phe Arg Thr Gln Thr Cys Pro Ile Met Ala Ser Trp Asp Leu Val Asn  
65 70 75 80

Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys  
85 90 95

Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser  
100 105 110

Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr  
115 120 125

Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln  
130 135 140

Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp  
145 150 155 160

Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu  
165 170 175

Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe  
180 185 190

Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile  
195 200 205

Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly  
210 215 220

Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg  
225 230 235 240

Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met  
245 250 255

Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr  
260 265 270

Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Tyr

275

280

285

Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn Gly Cys  
290 295 300

His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys  
305 310 315 320

Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile  
325 330 335

Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu Lys Ala  
340 345 350

Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly  
355 360 365

Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp  
370 375 380

Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro  
385 390 395 400

Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys  
405 410 415

Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys  
420 425 430

Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala  
435 440 445

Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn  
450 455 460

Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn  
465 470 475 480

Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Lys Ser Lys Pro Arg  
485 490 495

Leu Arg Asp Thr Ile Ile Gln Val Thr Trp Leu Glu Asn Gly Arg Ile  
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Lys Val Glu Ser Lys Asp Val Thr Asp Gly Lys Ala Ser Ser His Met  
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Leu Val Val Leu Lys Ser Ala Asp Leu Gln Glu Val Met Phe Thr Ala  
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Leu Ile Lys Asp Arg Pro Lys Phe Val Arg Leu Phe Leu Glu Asn Gly  
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Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu Phe  
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Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala Lys  
580 585 590

Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val Ala  
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Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp Glu  
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Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro Leu  
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Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu Ser  
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Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu Gly  
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Ala Ser Lys Leu Leu Lys Thr Leu Ala Lys Val Lys Asn Asp Ile Asn  
675 680 685

Ala Ala Gly Glu Ser Glu Glu Leu Ala Asn Glu Tyr Glu Thr Arg Ala  
690 695 700

Val Gly Glu Ser Thr Val Trp Asn Ala Val Val Gly Ala Asp Leu Pro  
705 710 715 720

Cys Gly Thr Asp Ile Ala Ser Gly Thr His Arg Pro Asp Gly Glu  
725 730 735

Leu Phe Thr Glu Cys Tyr Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu  
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Leu Val Tyr Ser Cys Glu Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu  
755 760 765

Ala Val Glu Ala Thr Asp Gln His Phe Ile Ala Gln Pro Gly Val Gln  
770 775 780

Asn Phe Leu Ser Lys Gln Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys  
785 790 795 800

Asn Trp Lys Ile Ile Leu Cys Leu Phe Ile Ile Pro Leu Val Gly Cys  
805 810 815

Gly Phe Val Ser Phe Arg Lys Lys Pro Val Asp Lys His Lys Lys Leu  
820 825 830

Leu Trp Tyr Tyr Val Ala Phe Phe Thr Ser Pro Phe Val Val Phe Ser  
835 840 845

Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val  
850 855 860

Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu Leu Val Leu  
865 870 875 880

Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Lys Arg Lys Thr Ala  
885 890 895

Met Asp Gln Thr Asp Glu Asp Leu Phe Pro Tyr Gly Ala Phe Tyr Gln  
900 905 910

Phe Leu Met Ile Ser Arg Ser Phe Arg Gly Glu Glu Met Ser Ile Gly  
915 920 925

Lys Gln His  
930